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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,724	10/01/2001	Kenneth W. Kinzler	01107.00193	3707
22907 7590 01/24/2007 BANNER & WITCOFF 1001 G STREET N W SUITE 1100 WASHINGTON, DC 20001			EXAMINER WHITEMAN, BRIAN A	
			ART UNIT 1635	PAPER NUMBER
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		01/24/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 09/966,724	<b>Applicant(s)</b> KINZLER ET AL.	
	<b>Examiner</b> Brian Whiteman	<b>Art Unit</b> 1635	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 November 2006.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 27,28,56,62 and 63 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 27,28,56,62,63 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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**! DETAILED ACTION**

Claims 27, 28, 56 and 62-63 are pending.

Applicant's traversal and the amendment to claims 27, 56, 62, and 63 in paper filed on 11/13/06 is acknowledged and considered.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27, 28, 56, 62 and 63 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 27, 28, 56, 62, and 63, as best understood, are readable on a genus of antisense oligonucleotides which are complementary to a coding sequence for human MDM2 and which inhibit expression of MDM2 protein, wherein the genus of oligonucleotides is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates a genus of antisense oligonucleotides, which bind to the hMDM2 gene or mRNA and prevent transcription or translation (page 10). The specification discloses SEQ ID NO: 2 (Figure 1), which is the cDNA for human MDM2. The instant specification does not disclose a nucleotide sequence comprising the human MDM2 gene. The prior art does not disclose the nucleotide sequence for the human MDM2 gene. Branch teaches, "internal structures of target RNAs and their association with cellular proteins create physical barriers, which render most potential binding sites inaccessible to antisense molecules (page 45 cited on PTO892). Gerwitz et al. (PNAS, 93:3161-3163, 1996) teach that mRNA targeting is to some extent a hit or miss process, accounting for many experiments in which the addition of an ODN yields no effect on expression (page 3161)." Uhlmann et al. teach, "It is clear from most in vitro studies that antisense oligonucleotides act most efficiently when directed against the initial part of the 5' non-coding region near the cap structure and against the region around the translation start codon (page 576)." (Chemical Review, 90: 544-84, 1990, cited on a PTO1449). Uhlmann et al. further teach, "Every mRNA has an individual secondary and tertiary structure that has a crucial influence on the efficiency of the target sequences" (page 576). "Although mRNA secondary structures can be calculated the efficiency of antisense oligonucleotides as inhibitors of protein translation has to be determined experimentally in practice" (page 576). While, one skilled in the art can envision a sequence that binds to SEQ ID NO: 2, the skilled artisan would be unable to determine without further experimentation if the sequence had a function that was considered essential for the claimed genus of oligonucleotides. There is a variation among species of the claimed genus of oligonucleotides. In addition, the skilled artisan understands that human MDM2 with polymorphisms are embraced by the claimed genus that are

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not disclosed in the instant specification or prior art. Furthermore, the specification does not disclose how to make a sufficient number of species to represent the genus of claimed oligonucleotides. The specification does not make any oligonucleotides embraced by the claimed genus. The only disclosure is part of paragraph in the specification contemplating an antisense oligonucleotide to hMDM2 gene or mRNA (bottom of page 10). Thus, the specification does not disclose how to make oligonucleotides that bind to human MDM2 which inhibit expression of MDM2 protein. The mere contemplation of the claimed genus in the specification is not sufficient to support the present claimed invention directed to a genus of antisense oligonucleotides. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of antisense oligonucleotides that must possess the biological properties as contemplated by applicants' disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CAFC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of antisense oligonucleotides that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has

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occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 11/13/06 have been fully considered but they are not persuasive.

In response to applicant's argument that the claims meet the written description requirement because the amended claims recite "a coding sequence for human MDM2", the argument is not found persuasive because the applicant is trying to claim antisense oligonucleotides that were not known until several years after the application was filed. See *Fiers v. Revel*, 25 USPQ2d 1601 (CAFC 1993). There is nothing in the specification that would direct the skilled artisan to the antisense compounds made after the filing date of the instant application. The generic contemplation of antisense in the specification (page 10, lined 25-28) does not provide guidance for the skilled artisan to make the antisense oligonucleotides taught in the post-filing articles.

In response to applicant's argument that the specification teaches assays which MDM2 expression can be detected, the argument is not found persuasive because, at the time of filing, antibodies to detect MDM2 proteins were not considered an assay for screening for antisense oligonucleotides. Antibodies are proteins and they are not nucleic acids. The screening method for antibodies is distinct and does not reasonably correlate to determining which antisense oligonucleotides would inhibit the expression of human MDM2.

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Furthermore, other than the applicant's assertion "The skilled worker would therefore easily have been able to use the assays and antibodies disclosed in the specification to test whether any particular oligonucleotide inhibited expression of MDM2 protein or interfere with expression of MDM2", there is no evidence of record to support applicant's assertion. See MPEP 716.01(c).

In response to the post-filing references supporting written description for the claimed invention, the argument is not found persuasive and has already been addressed in previous office actions. See office action mailed on 8/15/06.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 recites the limitation "the human MDM2 gene" in line 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (571) 272-0764. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas Schultz, PhD, SPE – Art Unit 1635, can be reached at (571) 272-0763.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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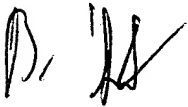
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Brian Whiteman

A handwritten signature in black ink, appearing to read 'B. Whiteman', located below the printed name.